

WHAT IS CLAIMED IS:

1. A composition comprising two appetite suppressants, wherein each appetite suppressant is selected from the group consisting of

- 5 (1) a 5HT transporter inhibitor;
- (2) a NE transporter inhibitor;
- (3) a CB-1 antagonist/inverse agonist;
- (4) a ghrelin antagonist;
- (5) a H3 antagonist/inverse agonist;
- 10 (6) a MCH1R antagonist;
- (7) a MCH2R agonist/antagonist;
- (8) a NPY1 antagonist;
- (9) a NPY2 agonist;
- (10) a NPY4 agonist;
- 15 (11) a mGluR5 antagonist;
- (12) leptin;
- (13) a leptin agonist/modulator;
- (14) a leptin derivative;
- (15) an opioid antagonist;
- 20 (16) an orexin antagonist;
- (17) a BRS3 agonist;
- (18) a CCK-A agonist;
- (19) CNTF;
- (20) a CNTF agonist/modulator;
- 25 (21) a CNTF derivative;
- (22) a 5HT2c agonist;
- (23) a Mc4r agonist;
- (24) a monoamine reuptake inhibitor;
- (25) a serotonin reuptake inhibitor;
- 30 (26) a GLP-1 agonist;
- (27) axokine;
- (28) fenfluramine;
- (29) nalmafene;
- (30) phentermine;
- 35 (31) rimonabant;

- (32) sibutramine;
- (33) topiramate; and
- (34) phytopharm compound 57;

and pharmaceutically acceptable salts and esters thereof;

5 provided that when the first appetite suppressant is a NPY1 antagonist, then the second appetite suppressant is not selected from the group consisting of: a MCH1R antagonist, a MCH2R antagonist, leptin, a leptin derivative, 5HT2c agonist, a Mc4r agonist, a serotonin reuptake inhibitor, and a GLP-1 agonist;

provided that when the first appetite suppressant is leptin, then the second appetite suppressant is
 10 not selected from the group consisting of: a MCH-1R antagonist, a MCH-2R antagonist, a NPY1 antagonist, a leptin derivative, 5HT2c agonist, a Mc4r agonist, a serotonin reuptake inhibitor, a GLP-1 agonist, a CCK-A agonist, an opioid antagonist, and a monoamine reuptake inhibitor;
 provided that when the first appetite suppressant is a CB-1 antagonist/inverse agonist, then the
 second appetite suppressant is not selected from the group consisting of: an opioid antagonist, a
 15 serotonin reuptake inhibitor, and a monoamine reuptake inhibitor; provided that when the first
 appetite suppressant is an opioid antagonist, then the second appetite suppressant is not a
 serotonin reuptake inhibitor; and
 provided that the appetite suppressants have different biological mechanisms of action.

20 2. The composition of Claim 1 wherein the appetite suppressant is selected from the group consisting of

- (1) a 5HT transporter inhibitor;
- (2) a NE transporter inhibitor;
- (3) a CB-1 antagonist/inverse agonist;
- 25 (4) a ghrelin antagonist;
- (5) a H3 antagonist/inverse agonist;
- (6) a MCH1R antagonist;
- (7) a MCH2R agonist/antagonist;
- (8) a NPY1 antagonist;
- 30 (9) a NPY2 agonist;
- (10) a NPY4 agonist;
- (11) a mGluR5 antagonist;
- (12) an opioid antagonist;
- (13) an orexin antagonist;
- 35 (14) a BRS3 agonist;

- 5 (15) a CCK-A agonist;
 (16) CNTF;
 (17) a CNTF agonist/modulator;
 (18) a CNTF derivative;
 (19) a 5HT2c agonist;
 (20) a Mc4r agonist;
 (21) a monoamine reuptake inhibitor;
 (22) a serotonin reuptake inhibitor;
 (23) a GLP-1 agonist;
 10 (24) axokine;
 (25) fenfluramine;
 (26) nalmafene;
 (27) phentermine;
 (28) rimonabant;
 15 (29) sibutramine; and
 (30) topiramate;

and pharmaceutically acceptable salts and esters thereof;

- provided that when the first appetite suppressant is a NPY1 antagonist, then the second appetite suppressant is not selected from the group consisting of: a MCH1R antagonist, a MCH2R
 20 antagonist, 5HT2c agonist, a Mc4r agonist, a serotonin reuptake inhibitor, and a GLP-1 agonist;
 provided that when the first appetite suppressant is a CB-1 antagonist/inverse agonist, then the second appetite suppressant is not selected from the group consisting of an opioid antagonist, a serotonin reuptake inhibitor, and a monoamine reuptake inhibitor;
 provided that when the first appetite suppressant is an opioid antagonist, then the second appetite
 25 suppressant is not a serotonin reuptake inhibitor; and
 provided that the appetite suppressants have different biological mechanisms of action.

3. The composition of Claim 2 wherein the first appetite suppressant is a Mc4r agonist, and pharmaceutically acceptable salts and esters thereof, and the second appetite
 30 suppressant is selected from the group consisting of
 (1) a MCH1R antagonist; and
 (2) a MCH2R agonist/antagonist;
 and pharmaceutically acceptable salts and esters thereof.

4. The composition of Claim 2 wherein the first appetite suppressant is a CB-1 antagonist/inverse agonist, and pharmaceutically acceptable salts and esters thereof, and the second appetite suppressant is selected from the group consisting of

- (1) a NPY1 antagonist;
- (2) a NPY2 agonist;
- (3) a NPY4 agonist;
- (4) a MCH1R antagonist;
- (5) a MCH2R agonist/antagonist; and
- (6) a Mc4r agonist;

and pharmaceutically acceptable salts and esters thereof.

5. The composition of Claim 1 further comprising a pharmaceutically acceptable carrier.

6. A method of treating a subject having a disorder associated with excessive food intake comprising administration of a therapeutically effective amount of two appetite suppressants selected from the group consisting of

- (1) a 5HT transporter inhibitor;
- (2) a NE transporter inhibitor;
- (3) a CB-1 antagonist/inverse agonist;
- (4) a ghrelin antagonist;
- (5) a H3 antagonist/inverse agonist;
- (6) a MCH1R antagonist;
- (7) a MCH2R agonist/antagonist;
- (8) a NPY1 antagonist;
- (9) a NPY2 agonist;
- (10) a NPY4 agonist;
- (11) a mGluR5 antagonist;
- (12) leptin;
- (13) a leptin agonist/modulator;
- (14) a leptin derivative;
- (15) an opioid antagonist;
- (16) an orexin antagonist;
- (17) a BRS3 agonist;
- (18) a CCK-A agonist;

- (19) CNTF;
- (20) a CNTF agonist/modulator;
- (21) a CNTF derivative;
- (22) a 5HT2c agonist;
- (23) a Mc4r agonist;
- (24) a monoamine reuptake inhibitor;
- (25) a serotonin reuptake inhibitor;
- (26) a GLP-1 agonist;
- (27) axokine;
- (28) fenfluramine;
- (29) nalmafene;
- (30) phentermine;
- (31) rimonabant;
- (32) sibutramine;
- (33) topiramate; and
- (34) phytopharm compound 57;

and pharmaceutically acceptable salts and esters thereof;

to a subject in need of such treatment;

provided that when the first appetite suppressant is a NPY1 antagonist, then the second appetite suppressant is not selected from the group consisting of: a MCH1R antagonist, a MCH2R antagonist, leptin, a leptin derivative, 5HT2c agonist, a Mc4r agonist, a serotonin reuptake inhibitor, and a GLP-1 agonist;

provided that when the first appetite suppressant is leptin, then the second appetite suppressant is not selected from the group consisting of: a MCH-1R antagonist, a MCH-2R antagonist, a NPY1 antagonist, a leptin derivative, 5HT2c agonist, a Mc4r agonist, a serotonin reuptake inhibitor, a GLP-1 agonist, a CCK-A agonist, an opioid antagonist, and a monoamine reuptake inhibitor;

provided that when the first appetite suppressant is a CB-1 antagonist/inverse agonist, then the second appetite suppressant is not selected from the group consisting of an opioid antagonist, a serotonin reuptake inhibitor, and a monoamine reuptake inhibitor; and provided that the appetite suppressants have different biological mechanisms of action.

7. The method according to Claim 6 wherein the disorder associated with excessive food intake is obesity.

8. The method according to Claim 7 wherein the disorder associated with excessive food intake is an obesity-related disorder.

5 9. The method according to Claim 8 wherein the obesity-related disorder is selected from: overeating; bulimia; hypertension; diabetes, elevated plasma insulin concentrations; insulin resistance; dyslipidemia; hyperlipidemia; endometrial, breast, prostate and colon cancer; osteoarthritis; obstructive sleep apnea; cholelithiasis; gallstones; coronary heart disease; abnormal heart rhythms; heart arrhythmias; myocardial infarction; polycystic ovary disease; craniopharyngioma; the Prader-Willi Syndrome; Frohlich's syndrome; GH-deficient
10 subjects; normal variant short stature; Turner's syndrome; metabolic syndrome; and acute lymphoblastic leukemia.

10. The method according to Claim 9 wherein the obesity-related disorder is diabetes.

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11. A composition comprising
(a) an appetite suppressant selected from the group consisting of

- (1) a 5HT transporter inhibitor;
- (2) a NE transporter inhibitor;
- 20 (3) a CB-1 antagonist/inverse agonist;
- (4) a ghrelin antagonist;
- (5) a H3 antagonist/inverse agonist;
- (6) a MCH1R antagonist;
- (7) a MCH2R agonist/antagonist;
- 25 (8) a NPY1 antagonist;
- (9) a NPY2 agonist;
- (10) a NPY4 agonist;
- (11) a mGluR5 antagonist;
- (12) leptin;
- 30 (13) a leptin derivative;
- (14) a leptin agonist/modulator;
- (15) an opioid antagonist;
- (16) an orexin antagonist;
- (17) a BRS3 agonist;
- 35 (18) a CCK-A agonist;

- 5 (19) CNTF;
 (20) a CNTF agonist/modulator;
 (21) a CNTF derivative;
 (22) 5HT2c agonist;
 (23) a Mc4r agonist;
 (24) a monoamine reuptake inhibitor;
 (25) a serotonin reuptake inhibitor;
 (26) a GLP-1 agonist;
 (27) axokine;
 10 (28) fenfluramine;
 (29) nalmafene;
 (30) phentermine;
 (31) rimonabant;
 (32) sibutramine;
 15 (33) topiramate; and
 (34) phytopharm compound 57;
 and pharmaceutically acceptable salts and esters thereof; and
 (b) a metabolic rate enhancer selected from the group consisting of
 20 (1) an ACC2 inhibitor;
 (2) a β 3 agonist;
 (3) a DGAT1 inhibitor;
 (4) a DGAT2 inhibitor;
 (5) a FAS inhibitor;
 (6) a PDE inhibitor;
 25 (7) a thyroid hormone β agonist;
 (8) an UCP-1, 2, or 3 activator;
 (9) an acyl-estrogen;
 (10) a glucocorticoid antagonist;
 (11) an 11 β HSD-1 inhibitor;
 30 (12) a Mc3r agonist;
 (13) a SCD-1;
 (14) oleoyl-estrone;
 (15) 3-[(3,5,7-trimethyl-1-adamantyl)methyl]-6,7,8,9-tetrahydro-5*H*-[1,2,4]
 triazolo[4,3-*a*]azepine;
 35 (16) 3-(1-adamantyl)-4-ethyl-5-(ethylthio)-4*H*-1,2,4-triazole;

(17) 3-adamantanyl-4,5,6,7,8,9,10,11,12,3a-decahydro-1,2,4-triazolo[4,3-a][11]annulene; and

(18) 3-(1-adamantyl)-5-(3,4,5-trimethoxyphenyl)-4-methyl-4H-1,2,4-triazole;

and pharmaceutically acceptable salts and esters thereof;

5 provided that when the metabolic rate enhancer is a $\beta 3$ agonist, then the appetite suppressant is not selected from the group consisting of: a CB-1 antagonist/inverse agonist, a MCH1R antagonist, a MCH2R antagonist, leptin, a leptin derivative, a CCK-A agonist, a 5HT2c agonist, a Mc4r agonist, a monoamine reuptake inhibitor, a serotonin reuptake inhibitor, and a GLP-1 agonist;

10 provided that when the metabolic rate enhancer is a UCP-1, 2 or 3 activator, then the appetite suppressant is not selected from the group consisting of: leptin, and a leptin derivative;

provided that when the metabolic rate enhancer is an 11β HSD-1 inhibitor, then the appetite suppressant is not selected from the group consisting of: a CB-1 antagonist/inverse agonist, a Mc4r agonist, a monoamine reuptake inhibitor, and a serotonin reuptake inhibitor; and

15 provided that when the appetite suppressant is a monoamine reuptake inhibitor, then the metabolic rate enhancer is not a PDE inhibitor.

12. A composition comprising an appetite suppressant selected from the group consisting of: a NPY5 antagonist, and pharmaceutically acceptable salts and esters thereof; and
20 metabolic rate enhancer selected from the group consisting of: an 11β HSD-1 inhibitor, and pharmaceutically acceptable salts and esters there.

13. The composition of Claim 12 further comprising a
25 pharmaceutically acceptable carrier.

14. A method of treating a subject having a disorder associated with excessive food intake comprising administration of

(a) a therapeutically effective amount of an appetite suppressant selected from the group consisting of

- 30
- (1) a 5HT transporter inhibitor;
 - (2) a NE transporter inhibitor;
 - (3) a CB-1 antagonist/inverse agonist;
 - (4) a ghrelin antagonist;
 - (5) a H3 antagonist/inverse agonist;
 - 35 (6) a MCH1R antagonist;

- (7) a MCH2R agonist/antagonist;
 (8) a NPY1 antagonist;
 (9) a NPY2 agonist;
 (10) a NPY4 agonist;
 5 (11) a mGluR5 antagonist;
 (12) leptin;
 (13) a leptin agonist/modulator;
 (14) a leptin derivative;
 (15) an opioid antagonist;
 10 (16) an orexin antagonist;
 (17) a BRS3 agonist;
 (18) a CCK-A agonist;
 (19) CNTF;
 (20) a CNTF agonist/modulator;
 15 (21) a CNTF derivative;
 (22) 5HT2c agonist;
 (23) a Mc4r agonist;
 (24) a monoamine reuptake inhibitor;
 (25) a serotonin reuptake inhibitor;
 20 (26) a GLP-1 agonist;
 (27) axokine;
 (28) fenfluramine;
 (29) nalmafene;
 (30) phentermine;
 25 (31) rimonabant;
 (32) sibutramine;
 (33) topiramate; and
 (34) phytopharm compound 57;
 and pharmaceutically acceptable salts and esters thereof; and
 30 (b) a therapeutically effective amount of a metabolic rate enhancer selected from the group
 consisting of
 (1) an ACC2 inhibitor;
 (2) a β 3 agonist;
 (3) a DGAT1 inhibitor;
 35 (4) a DGAT2 inhibitor;

- (5) a FAS inhibitor;
- (6) a PDE inhibitor;
- (7) a thyroid hormone β agonist;
- (8) an UCP-1, 2, or 3 activator;
- 5 (9) an acyl-estrogen;
- (10) a glucocorticoid antagonist;
- (11) an 11β HSD-1 inhibitor;
- (12) a Mc3r agonist;
- (13) a SCD-1;
- 10 (14) oleoyl-estrone;
- (15) 3-[(3,5,7-trimethyl-1-adamantyl)methyl]-6,7,8,9-tetrahydro-5*H*-[1,2,4]triazolo[4,3-*a*]azepine;
- (16) 3-(1-adamantyl)-4-ethyl-5-(ethylthio)-4*H*-1,2,4-triazole;
- (17) 3-adamantany-4,5,6,7,8,9,10,11,12,3a-decahydro-1,2,4-triazolo[4,3-*a*][11]annulene; and
- 15 (18) 3-(1-adamantyl)-5-(3,4,5-trimethoxyphenyl)-4-methyl-4*H*-1,2,4-triazole;

and pharmaceutically acceptable salts and esters thereof;

to a subject in need of such treatment;

provided that when the metabolic rate enhancer is a $\beta 3$ agonist, then the appetite suppressant is not selected from the group consisting of: a CB-1 antagonist/inverse agonist, a MCH1R antagonist, a MCH2R antagonist, leptin, a leptin derivative, a CCK-A agonist, a 5HT2c agonist, a Mc4r agonist, a monoamine reuptake inhibitor, a serotonin reuptake inhibitor, and a GLP-1 agonist;

provided that when the metabolic rate enhancer is a UCP-1, 2 or 3 activator, then the appetite suppressant is not selected from the group consisting of: leptin, and a leptin derivative;

provided that when the metabolic rate enhancer is an 11β HSD-1 inhibitor, then the appetite suppressant is not selected from the group consisting of: a CB-1 antagonist/inverse agonist, a Mc4r agonist, a monoamine reuptake inhibitor, and a serotonin reuptake inhibitor; and

provided that when the appetite suppressant is a monoamine reuptake inhibitor, then the metabolic rate enhancer is not a PDE inhibitor.

15. The method according to Claim 14 wherein the disorder associated with excessive food intake is obesity.

16. The method according to Claim 15 wherein the disorder associated with excessive food intake is an obesity-related disorder.

17. The method according to Claim 16 wherein the obesity-related disorder is selected from: overeating; bulimia; hypertension; diabetes, elevated plasma insulin concentrations; insulin resistance; dyslipidemia; hyperlipidemia; endometrial, breast, prostate and colon cancer; osteoarthritis; obstructive sleep apnea; cholelithiasis; gallstones; coronary heart disease; abnormal heart rhythms; heart arrhythmias; myocardial infarction; polycystic ovary disease; craniopharyngioma; the Prader-Willi Syndrome; Frohlich's syndrome; GH-deficient subjects; normal variant short stature; Turner's syndrome; metabolic syndrome; and acute lymphoblastic leukemia.

18. The method according to Claim 17 wherein the obesity-related disorder is diabetes.

19. A composition comprising
(a) an appetite suppressant selected from the group consisting of

- (1) a 5HT transporter inhibitor;
- (2) a NE transporter inhibitor;
- (3) a CB-1 antagonist/inverse agonist;
- (4) a ghrelin antagonist;
- (5) a H3 antagonist/inverse agonist;
- (6) a MCH1R antagonist;
- (7) a MCH2R agonist/antagonist;
- (8) a NPY1 antagonist;
- (9) a NPY2 agonist;
- (10) a NPY4 agonist;
- (11) a mGluR5 antagonist;
- (12) leptin;
- (13) a leptin agonist/modulator;
- (14) a leptin derivative;
- (15) an opioid antagonist;
- (16) an orexin antagonist;
- (17) a BRS3 agonist;
- (18) a CCK-A agonist;

- (19) CNTF;
 (20) a CNTF agonist/modulator;
 (21) a CNTF derivative;
 (22) a 5HT_{2c} agonist;
 5 (23) a Mc4r agonist;
 (24) a monoamine reuptake inhibitor;
 (25) a serotonin reuptake inhibitor;
 (26) a GLP-1 agonist;
 (27) axokine;
 10 (28) fenfluramine;
 (29) nalmafene;
 (30) phentermine;
 (31) rimonabant;
 (32) sibutramine;
 15 (33) topiramate; and
 (34) phytopharm compound 57;
 and pharmaceutically acceptable salts and esters thereof; and
 (b) a nutrient absorption inhibitor selected from the group consisting of
 (1) a lipase inhibitor;
 20 (2) a fatty acid transporter inhibitor;
 (3) a dicarboxylate transporter inhibitor;
 (4) a glucose transporter inhibitor;
 (5) a phosphate transporter inhibitor; and
 (6) orlistat;
 25 and pharmaceutically acceptable salts and esters thereof;
 provided that when the appetite suppressant is a monoamine reuptake inhibitor, then the nutrient
 absorption inhibitor is not a lipase inhibitor.
20. The composition of Claim 19 further comprising a pharmaceutically
 30 acceptable carrier.
21. A method of treating a subject having a disorder associated with excessive
 food intake comprising administration of
 (a) a therapeutically effective amount of an appetite suppressant selected from the group
 35 consisting of

- (1) a 5HT transporter inhibitor;
- (2) a NE transporter inhibitor;
- (3) a CB-1 antagonist/inverse agonist;
- (4) a ghrelin antagonist;
- 5 (5) a H3 antagonist/inverse agonist;
- (6) a MCH1R antagonist;
- (7) a MCH2R agonist/antagonist;
- (8) a NPY1 antagonist;
- (9) a NPY2 agonist;
- 10 (10) a NPY4 agonist;
- (11) a mGluR5 antagonist;
- (12) leptin;
- (13) a leptin agonist/modulator;
- (14) a leptin derivative;
- 15 (15) an opioid antagonist;
- (16) an orexin antagonist;
- (17) a BRS3 agonist;
- (18) a CCK-A agonist;
- (19) CNTF;
- 20 (20) a CNTF agonist/modulator;
- (21) a CNTF derivative;
- (22) a 5HT2c agonist;
- (23) a Mc4r agonist;
- (24) a monoamine reuptake inhibitor;
- 25 (25) a serotonin reuptake inhibitor;
- (26) a GLP-1 agonist;
- (27) axokine;
- (28) fenfluramine;
- (29) nalmafene;
- 30 (30) phentermine;
- (31) rimonabant;
- (32) sibutramine;
- (33) topiramate; and
- (34) phytopharm compound 57;
- 35 and pharmaceutically acceptable salts and esters thereof; and

(b) a therapeutically effective amount of a nutrient absorption inhibitor selected from the group consisting of

- (1) a lipase inhibitor;
- (2) a fatty acid transporter inhibitor;
- (3) a dicarboxylate transporter inhibitor;
- (4) a glucose transporter inhibitor;
- (5) a phosphate transporter inhibitor; and
- (6) orlistat;

and pharmaceutically acceptable salts and esters thereof;

to a subject in need of such treatment;

provided that when the appetite suppressant is a monoamine reuptake inhibitor, then the nutrient absorption inhibitor is not a lipase inhibitor.

22. The method according to Claim 21 wherein the disorder associated with excessive food intake is obesity.

23. The method according to Claim 22 wherein the disorder associated with excessive food intake is an obesity-related disorder.

24. The method according to Claim 23 wherein the obesity-related disorder is selected from: overeating; bulimia; hypertension; diabetes, elevated plasma insulin concentrations; insulin resistance; dyslipidemia; hyperlipidemia; endometrial, breast, prostate and colon cancer; osteoarthritis; obstructive sleep apnea; cholelithiasis; gallstones; coronary heart disease; abnormal heart rhythms; heart arrhythmias; myocardial infarction; polycystic ovary disease; craniopharyngioma; the Prader-Willi Syndrome; Frohlich's syndrome; GH-deficient subjects; normal variant short stature; Turner's syndrome; metabolic syndrome; and acute lymphoblastic leukemia.

25. The method according to Claim 24 wherein the obesity-related disorder is diabetes.

26. A composition comprising two metabolic rate enhancers, wherein each metabolic rate enhancer is selected from the group consisting of

- (1) an ACC2 inhibitor;
- (2) a $\beta 3$ agonist;

- (3) a DGAT1 inhibitor;
 (4) a DGAT2 inhibitor;
 (5) a FAS inhibitor;
 (6) a PDE inhibitor;
 5 (7) a thyroid hormone β agonist;
 (8) an UCP-1, 2, or 3 activator;
 (9) an acyl-estrogen;
 (10) a glucocorticoid antagonist;
 (11) an 11β HSD-1 inhibitor;
 10 (12) a Mc3r agonist;
 (13) a SCD-1;
 (14) oleoyl-estrone;
 (15) 3-[(3,5,7-trimethyl-1-adamantyl)methyl]-6,7,8,9-tetrahydro-5*H*-[1,2,4]
 triazolo[4,3-*a*]azepine;
 15 (16) 3-(1-adamantyl)-4-ethyl-5-(ethylthio)-4*H*-1,2,4-triazole;
 (17) 3-adamantanyl-4,5,6,7,8,9,10,11,12,3*a*-decahydro-1,2,4-triazolo[4,3-
a][11]annulene; and
 (18) 3-(1-adamantyl)-5-(3,4,5-trimethoxyphenyl)-4-methyl-4*H*-1,2,4-triazole;
 and pharmaceutically acceptable salts and esters thereof;
 20 provided that when the first metabolic rate enhancer is an 11β HSD-1 inhibitor, then the second
 metabolic rate enhancer is not a β 3 agonist; and
 provided that the metabolic rate enhancers have different biological mechanisms of action.

25 27. The composition of Claim 26 further comprising a pharmaceutically
 acceptable carrier.

28. A method of treating a subject having a disorder associated with excessive
 food intake comprising administration of a therapeutically effective amount of two metabolic rate
 enhancers selected from the group consisting of
 30 (1) an ACC2 inhibitor;
 (2) a β 3 agonist;
 (3) a DGAT1 inhibitor;
 (4) a DGAT2 inhibitor;
 (5) a FAS inhibitor;
 35 (6) a PDE inhibitor;

- (7) a thyroid hormone β agonist;
- (8) an UCP-1, 2, or 3 activator;
- (9) an acyl-estrogen;
- (10) a glucocorticoid antagonist;
- (11) an 11β HSD-1 inhibitor;
- (12) a Mc3r agonist;
- (13) a SCD-1;
- (14) oleoyl-estrone;
- (15) 3-[(3,5,7-trimethyl-1-adamantyl)methyl]-6,7,8,9-tetrahydro-5*H*-[1,2,4] triazolo[4,3-*a*]azepine;
- (16) 3-(1-adamantyl)-4-ethyl-5-(ethylthio)-4*H*-1,2,4-triazole;
- (17) 3-adamantanyl-4,5,6,7,8,9,10,11,12,3a-decahydro-1,2,4-triazolo[4,3-*a*][11]annulene; and
- (18) 3-(1-adamantyl)-5-(3,4,5-trimethoxyphenyl)-4-methyl-4*H*-1,2,4-triazole;

and pharmaceutically acceptable salts and esters thereof;

to a subject in need of such treatment;

provided that when the first metabolic rate enhancer is an 11β HSD-1 inhibitor, then the second metabolic rate enhancer is not a $\beta 3$ agonist; and

provided that the metabolic rate enhancers have different biological mechanisms of action.

29. The method according to Claim 28 wherein the disorder associated with excessive food intake is obesity.

30. The method according to Claim 29 wherein the disorder associated with excessive food intake is an obesity-related disorder.

31. The method according to Claim 30 wherein the obesity-related disorder is selected from: overeating; bulimia; hypertension; diabetes, elevated plasma insulin concentrations; insulin resistance; dyslipidemia; hyperlipidemia; endometrial, breast, prostate and colon cancer; osteoarthritis; obstructive sleep apnea; cholelithiasis; gallstones; coronary heart disease; abnormal heart rhythms; heart arrhythmias; myocardial infarction; polycystic ovary disease; craniopharyngioma; the Prader-Willi Syndrome; Frohlich's syndrome; GH-deficient subjects; normal variant short stature; Turner's syndrome; metabolic syndrome; and acute lymphoblastic leukemia.

32. The method according to Claim 31 wherein the obesity-related disorder is diabetes.

33. A composition comprising a metabolic rate enhancer, and pharmaceutically acceptable salts and esters thereof, and a nutrient absorption inhibitor, and pharmaceutically acceptable salts and esters thereof.

34. The composition of Claim 33 comprising
(a) a metabolic rate enhancer selected from the group consisting of

- (1) an ACC2 inhibitor;
- (2) a β 3 agonist;
- (3) a DGAT1 inhibitor;
- (4) a DGAT2 inhibitor;
- (5) a FAS inhibitor;
- (6) a PDE inhibitor;
- (7) a thyroid hormone β agonist;
- (8) an UCP-1, 2, or 3 activator;
- (9) an acyl-estrogen;
- (10) a glucocorticoid antagonist;
- (11) an 11β HSD-1 inhibitor;
- (12) a Mc3r agonist;
- (13) a SCD-1;
- (14) oleoyl-estrone;
- (15) 3-[(3,5,7-trimethyl-1-adamantyl)methyl]-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepine;
- (16) 3-(1-adamantyl)-4-ethyl-5-(ethylthio)-4H-1,2,4-triazole;
- (17) 3-adamantanyl-4,5,6,7,8,9,10,11,12,3a-decahydro-1,2,4-triazolo[4,3-a][11]annulene; and
- (18) 3-(1-adamantyl)-5-(3,4,5-trimethoxyphenyl)-4-methyl-4H-1,2,4-triazole;

and pharmaceutically acceptable salts and esters thereof; and

(b) a nutrient absorption inhibitor selected from the group consisting of

- (1) a lipase inhibitor;
- (2) a fatty acid transporter inhibitor;
- (3) a dicarboxylate transporter inhibitor;
- (4) a glucose transporter inhibitor;

(5) a phosphate transporter inhibitor; and

(6) orlistat;

and pharmaceutically acceptable salts and esters thereof.

5 35. The composition of Claim 34 further comprising a pharmaceutically acceptable carrier.

36. A method of treating a subject having a disorder associated with excessive food intake comprising administration of

10 (a) a therapeutically effective amount of a metabolic rate enhancer selected from the group consisting of

(1) an ACC2 inhibitor;

(2) a β 3 agonist;

(3) a DGAT1 inhibitor;

15 (4) a DGAT2 inhibitor;

(5) a FAS inhibitor;

(6) a PDE inhibitor;

(7) a thyroid hormone β agonist;

(8) an UCP-1, 2, or 3 activator;

20 (9) an acyl-estrogen;

(10) a glucocorticoid antagonist;

(11) an 11β HSD-1 inhibitor;

(12) a Mc3r agonist;

(13) a SCD-1;

25 (14) oleoyl-estrone;

(15) 3-[(3,5,7-trimethyl-1-adamantyl)methyl]-6,7,8,9-tetrahydro-5H-[1,2,4] triazolo[4,3-*a*]azepine;

(16) 3-(1-adamantyl)-4-ethyl-5-(ethylthio)-4H-1,2,4-triazole;

(17) 3-adamantanyl-4,5,6,7,8,9,10,11,12,3a-decahydro-1,2,4-triazolo[4,3-*a*][11]annulene; and

30 (18) 3-(1-adamantyl)-5-(3,4,5-trimethoxyphenyl)-4-methyl-4H-1,2,4-triazole;

and pharmaceutically acceptable salts and esters thereof; and

(b) a therapeutically effective amount of a nutrient absorption inhibitor selected from the group consisting of

35 (1) a lipase inhibitor;

- (2) a fatty acid transporter inhibitor;
- (3) a dicarboxylate transporter inhibitor;
- (4) a glucose transporter inhibitor;
- (5) a phosphate transporter inhibitor; and
- (6) orlistat;

and pharmaceutically acceptable salts and esters thereof;
to a subject in need of such treatment.

37. The method according to Claim 36 wherein the disorder associated with excessive food intake is obesity.

38. The method according to Claim 37 wherein the disorder associated with excessive food intake is an obesity-related disorder.

39. The method according to Claim 38 wherein the obesity-related disorder is selected from: overeating; bulimia; hypertension; diabetes, elevated plasma insulin concentrations; insulin resistance; dyslipidemia; hyperlipidemia; endometrial, breast, prostate and colon cancer; osteoarthritis; obstructive sleep apnea; cholelithiasis; gallstones; coronary heart disease; abnormal heart rhythms; heart arrhythmias; myocardial infarction; polycystic ovary disease; craniopharyngioma; the Prader-Willi Syndrome; Frohlich's syndrome; GH-deficient subjects; normal variant short stature; Turner's syndrome; metabolic syndrome; and acute lymphoblastic leukemia.

40. The method according to Claim 39 wherein the obesity-related disorder is diabetes.

41. A composition comprising two nutrient absorption inhibitors, and pharmaceutically acceptable salts and esters thereof, provided that the nutrient absorption inhibitors have different biological mechanisms of action.

42. The composition of Claim 41, wherein each nutrient absorption inhibitor is selected from the group consisting of

- (1) a lipase inhibitor;
- (2) a fatty acid transporter inhibitor;
- (3) a dicarboxylate transporter inhibitor;

- (4) a glucose transporter inhibitor;
- (5) a phosphate transporter inhibitor; and
- (6) orlistat;

and pharmaceutically acceptable salts and esters thereof;

5 provided that the nutrient absorption inhibitors have different biological mechanisms of action.

43. The composition of Claim 42 further comprising a pharmaceutically acceptable carrier.

10 44. A method of treating a subject having a disorder associated with excessive food intake comprising administration of a therapeutically effective amount of two nutrient absorption inhibitors selected from the group consisting of

- (1) a lipase inhibitor;
- (2) a fatty acid transporter inhibitor;
- 15 (3) a dicarboxylate transporter inhibitor;
- (4) a glucose transporter inhibitor;
- (5) a phosphate transporter inhibitor; and
- (6) orlistat;

and pharmaceutically acceptable salts and esters thereof;

20 to a subject in need of such treatment;

provided that the nutrient absorption inhibitors have different biological mechanisms of action.

45. The method according to Claim 44 wherein the disorder associated with excessive food intake is obesity.

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46. The method according to Claim 45 wherein the disorder associated with excessive food intake is an obesity-related disorder.

30 47. The method according to Claim 46 wherein the obesity-related disorder is selected from: overeating; bulimia; hypertension; diabetes, elevated plasma insulin concentrations; insulin resistance; dyslipidemia; hyperlipidemia; endometrial, breast, prostate and colon cancer; osteoarthritis; obstructive sleep apnea; cholelithiasis; gallstones; coronary heart disease; abnormal heart rhythms; heart arrhythmias; myocardial infarction; polycystic ovary disease; craniopharyngioma; the Prader-Willi Syndrome; Frohlich's syndrome; GH-deficient

subjects; normal variant short stature; Turner's syndrome; metabolic syndrome; and acute lymphoblastic leukemia.

- 5 48. The method according to Claim 47 wherein the obesity-related disorder is
diabetes.